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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/988,285 | 11/19/2001 | Johannes Henricus Matthias Schellens | Q67353 | 8475 |

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EXAMINER

WEDDINGTON, KEVIN E

ART UNIT PAPER NUMBER

1614

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/988,285

Applicant(s)

SCHELLENS ET AL.

Examiner

Kevin E. Weddington

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 October 2004.
2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 and 30-34 is/are pending in the application.
4a) Of the above claim(s) 4,7-12,14 and 18-21 is/are withdrawn from consideration.
5) ☒ Claim(s) 30 and 31 is/are allowed.
6) ☒ Claim(s) 1-3,5,6,13,15-17,22,32 and 33 is/are rejected.
7) ☒ Claim(s) 34 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

Art Unit: 1614

Claims 1-22 and 30-34 are presented for examination.

Applicants' amendment filed October 25, 2004 has been received and entered.

Accordingly, the rejection made under 35 USC 112, second paragraph as set forth in the previous Office action dated June 24, 2004 at page 3 is hereby withdrawn.

Claims 4, 7-12, 14 and 18-21 are withdrawn from consideration as being drawn to the non-elected invention (37 CFR 1.142(b)).

Claim Objections

Claim 34 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Allowable Subject Matter

Claims 30 and 31 are allowable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5, 6, 13, 15-17, 22, 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing the bioavailability of topotecan, a cytostatic camptothecin derivative, a pharmaceutically active compound with GF120918, an inhibitor of BCRP, does not reasonably provide enablement for increasing the bioavailability of all

Art Unit: 1614

pharmaceutically active compounds combined with other inhibitors of BCRP of claims 5 and 13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. CIR., 1988) as to undue experimentation.

The factors include:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided
- 3) the presence or absence of working examples
- 4) the nature of the invention
- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to a method for increasing the bioavailability of an orally administered pharmaceutically active compound comprising:

orally administering a bioenhancer comprising an inhibitor of BCRP and said pharmaceutically active compound, wherein said inhibitor and said pharmaceutically active compound are concomitantly administered.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

The present invention is unpredictable unless experimentation is shown from the other bioenhancer compositions comprising other pharmaceutically active compounds combined with other inhibitors of BCRP.

The breadth of the claims

The claims are very broad and inclusive all combinations comprising a pharmaceutically active compound and an inhibitor of BCRP.

The amount of direction or guidance provided and the presence or absence of working examples

The working example is limited to the administration of a bioenhancer comprising toptecan and GF120918 for increasing bioavailability.

In Example 4, the applicants state novel substances XR9051 and XR9576 are considered alternatives of the already disclosed compound GF120918, however, there are no actual example showing the combination of the novel substances with a pharmaceutically active compound.

No example showing the other pharmaceutically compounds, especially indolozino-quinoline derivatives, camphothecin derivatives, anthraquinone derivative and quanzoline derivatives combine with other inhibitors of BCRP.

The quantity of experimentation necessary

Applicants have failed to provide guidance as how the bioenhancers comprising a combination of other pharmaceutically active compounds and other inhibitors of BCRP is effective in increasing bioavailability. The level of experimentation is needed to determine the other bioenhancers combinations. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

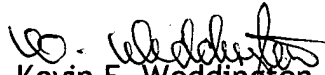
Claims 1-3, 5, 6, 13, 15-17, 22, 32 and 33 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1614

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Kevin E. Weddington
Primary Examiner
Art Unit 1614

K. Weddington
March 16, 2005